

### III. AMENDMENT OF THE CLAIMS

PLEASE ENTER THE FOLLOWING AMENDMENT WITHOUT PREJUDICE OR DISCLAIMER. Applicants reserve the right to file a divisional or continuation application to the originally filed claims.

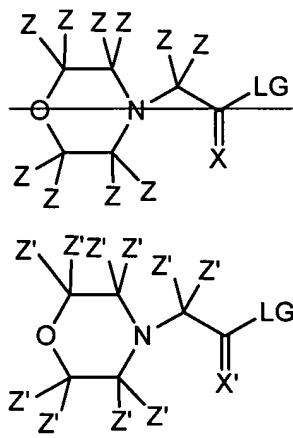
#### Claim 1 (Canceled)

2. (Currently Amended) The compound of claim 71, wherein the compound is isotopically enriched with three or more heavy atom isotopes.
3. (Currently Amended) The compound of claim 71, wherein the six-membered heterocyclic ring is substituted with one or more substituents.
4. (Original) The compound of claim 3, wherein the one or more substituents are alkyl, alkoxy or aryl groups.
5. (Original) The compound of claim 4, wherein the one or more substituents are protected or unprotected amine groups, hydroxyl groups or thiol groups.

#### Claims 6-7 (Canceled)

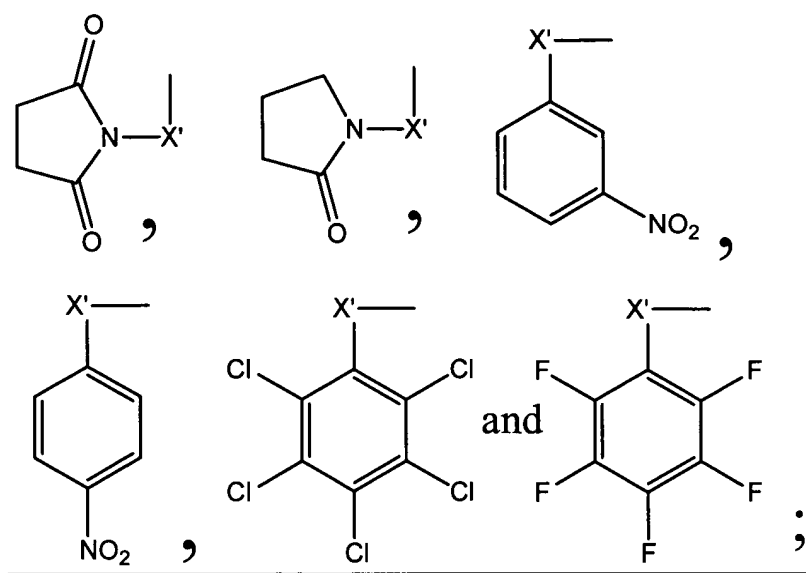
8. (Currently Amended) The compound of claim 71, wherein the six-membered heterocyclic ring comprises one or more additional nitrogen, oxygen or sulfur atoms.
9. (Currently Amended) The compound of claim 71, wherein ~~active ester is an N-hydroxysuccinimide ester~~ LG is N-hydroxysuccinimide.
10. (Currently Amended) The compound of claim 71, wherein the compound is a salt.

11. (Currently Amended) The compound of claim 71, wherein the compound is a mono-TFA salt, a mono-HCl salt, a bis-TFA salt or a bis-HCl salt.
12. (Currently Amended) The compound of claim 71, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity.
13. (Currently Amended) The compound of claim 71, wherein each incorporated heavy atom isotope is present in at least 93 percent isotopic purity.
14. (Currently Amended) The compound of claim 71, wherein each incorporated heavy atom isotope is present in at least 96 percent isotopic purity.
15. (Currently Amended) An N-substituted morpholine acetic acid active ester compound of the formula:



or a salt thereof, wherein;

LG is the leaving group of an active ester selected from the group consisting of:



X' is O or S;

each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms;  
and

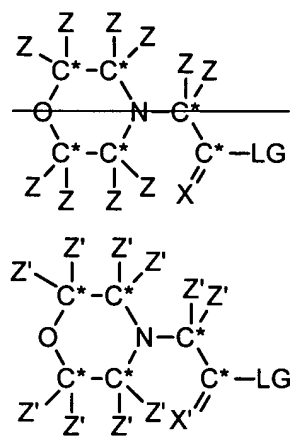
wherein the N-substituted morpholine acetic acid active ester is isotopically enriched with one or more heavy atom isotopes.

16. (Original) The compound of claim 15, wherein the N-substituted morpholine acetic acid active ester is isotopically enriched with three or more heavy atom isotopes.

Claim 17 (Canceled)

18. (Currently Amended) The compound of claim 15, wherein LG is N-hydroxysuccinimide.
19. (Currently Amended) The compound of claim 15, wherein each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine or iodine.

20. (Currently Amended) The compound of claim 15, wherein each  $Z'_$  is independently hydrogen, methyl or methoxy.
21. (Currently Amended) The compound of claim 15, wherein  $X'_$  is  $^{16}\text{O}$  or  $^{18}\text{O}$ .
22. (Original) The compound of claim 15, wherein the nitrogen atom of the morpholine ring is  $^{14}\text{N}$  or  $^{15}\text{N}$ .
23. (Currently Amended) The compound of claim 15, of the formula:



wherein;

each  $C^*$  is independently  $^{12}\text{C}$  or  $^{13}\text{C}$ ;

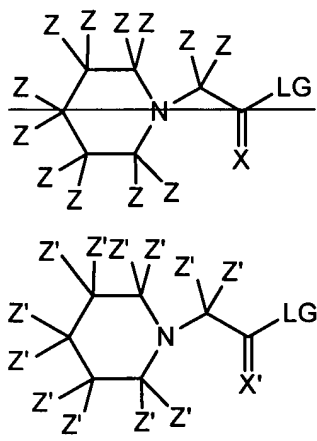
LG is the leaving group of an active ester as defined in claim 15;

$X'_$  is O or S; and

each  $Z'_$  is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms.

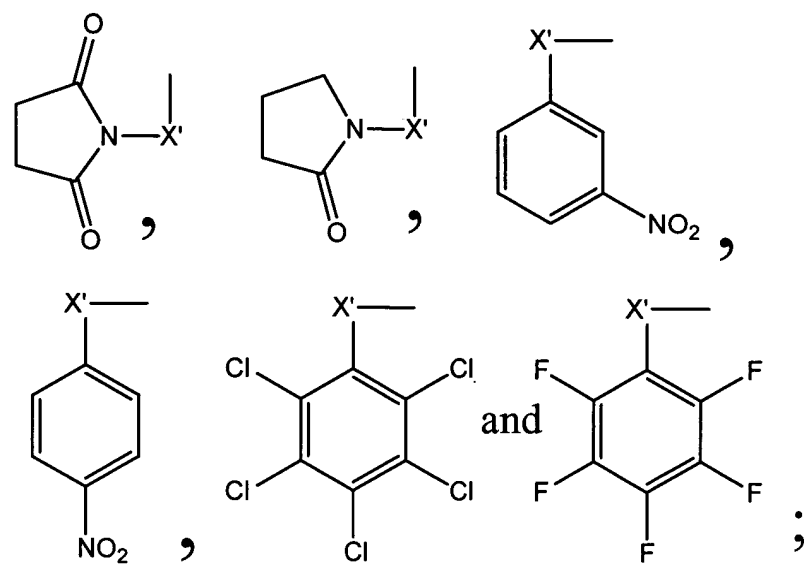
24. (Original) The compound of claim 15, wherein the compound is a mono-TFA salt or a mono-HCl salt.

25. (Original) The compound of claim 15, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity.
26. (Original) The compound of claim 15, wherein each incorporated heavy atom isotope is present in at least 93 percent or isotopic purity.
27. (Original) The compound of claim 15, wherein each incorporated heavy atom isotope is present in at least 96 percent or isotopic purity.
28. (Currently Amended) An N-substituted piperidine acetic acid active ester compound of the formula:



or a salt thereof, wherein;

LG is the leaving group of an active ester selected from the group consisting of:



X' is O or S;

each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms;  
and

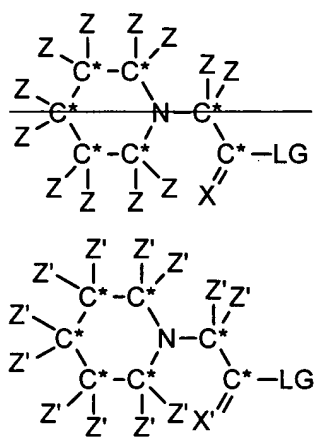
wherein the N-substituted piperidine acetic acid active ester is isotopically enriched with one or more heavy atom isotopes.

29. (Original) The compound of claim 28, wherein the N-substituted piperidine acetic acid active ester is isotopically enriched with three or more heavy atom isotopes.

Claim 30 (Canceled)

31. (Original) The compound of claim 28, wherein LG is N-hydroxysuccinimide.
32. (Currently Amended) The compound of claim 28, wherein each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine or iodine.

33. (Currently Amended) The compound of claim 28, wherein each  $Z'_$  is independently hydrogen, methyl or methoxy.
34. (Currently Amended) The compound of claim 28, wherein  $X'_$  is  $^{16}\text{O}$  or  $^{18}\text{O}$ .
35. (Original) The compound of claim 28, wherein the nitrogen atom of the piperidine ring is  $^{14}\text{N}$  or  $^{15}\text{N}$ .
36. (Currently Amended) The compound of claim 28, of the formula:



wherein;

each  $C^*$  is independently  $^{12}\text{C}$  or  $^{13}\text{C}$ ;

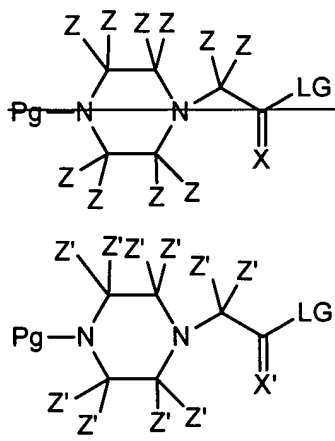
LG is the leaving group of an active ester as defined in claim 28;

$X'_$  is O or S; and

each  $Z'_$  is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms.

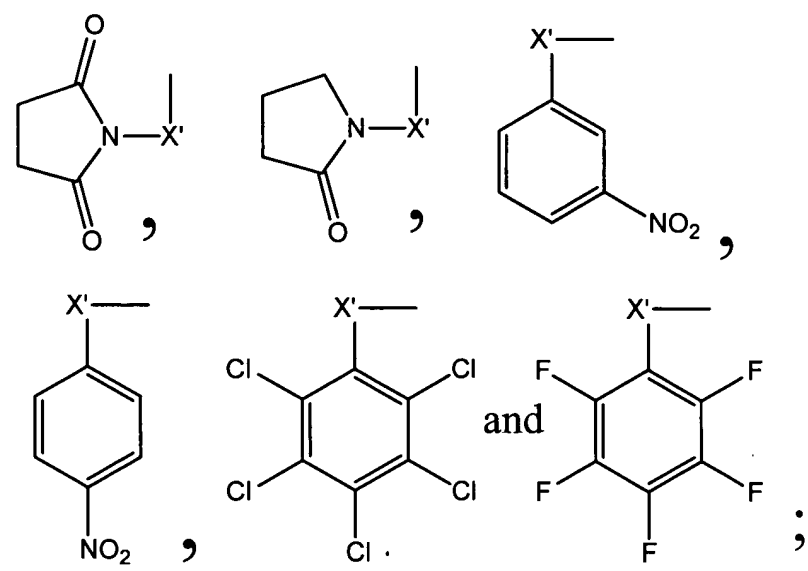
37. (Original) The compound of claim 28, wherein the compound is a mono-TFA salt or a mono-HCl salt.

38. (Original) The compound of claim 28, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity.
39. (Original) The compound of claim 28, wherein each incorporated heavy atom isotope is present in at least 93 percent or isotopic purity.
40. (Original) The compound of claim 28, wherein each incorporated heavy atom isotope is present in at least 96 percent or isotopic purity.
41. (Currently Amended) An N-substituted piperazine acetic acid active ester compound of the formula:



or a salt thereof, wherein;

LG is the leaving group of an active ester selected from the group consisting of:



X' is O or S;

Pg is an amine-protecting group;

each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms; and

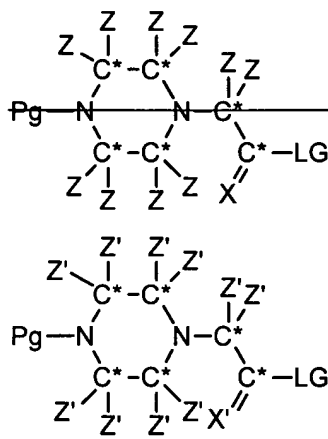
wherein the N-substituted piperazine acetic acid active ester is isotopically enriched with one or more heavy atom isotopes.

42. (Currently Amended) The compound of claim 41, wherein the N-substituted piperazine acetic acid active ester is isotopically enriched with three or more heavy atom isotopes.

Claim 43 (Canceled)

44. (Original) The compound of claim 41, wherein LG is N-hydroxysuccinimide.
45. (Currently Amended) The compound of claim 41, wherein each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine or iodine.

46. (Currently Amended) The compound of claim 41, wherein each Z' is independently hydrogen, methyl or methoxy.
47. (Currently Amended) The compound of claim 41, wherein X' is <sup>16</sup>O or <sup>18</sup>O.
48. (Original) The compound of claim 41, wherein each nitrogen atom of the piperazine ring is <sup>14</sup>N or <sup>15</sup>N.
49. (Currently Amended) The compound of claim 41, of the formula:



wherein,

each  $C^*$  is independently  $^{12}\text{C}$  or  $^{13}\text{C}$ ;

LG is the leaving group of an active ester as defined in claim 41;

$X'$  is O or S;

Pg is an amine protecting group; and

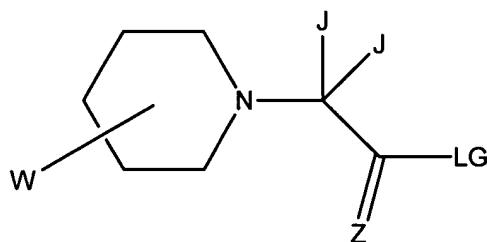
each Z' is independently hydrogen, deuterium, fluorine, chlorine, bromine, iodine, an amino acid side chain or a straight chain or branched C1-C6 alkyl group that may optionally contain a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups each independently comprise linked hydrogen, deuterium or fluorine atoms.

50. (Currently Amended) The compound of claim 41, wherein the compound is a mono-TFA salt, a mono-HCl salt, a bis-TFA salt or a bis-HCl salt.

51. (Original) The compound of claim 41, wherein each incorporated heavy atom isotope is present in at least 80 percent isotopic purity.
52. (Original) The compound of claim 41, wherein each incorporated heavy atom isotope is present in at least 93 percent or isotopic purity.
53. (Original) The compound of claim 41, wherein each incorporated heavy atom isotope is present in at least 96 percent or isotopic purity.

Claims 54-70 (Canceled)

71. (New) A compound of formula:



wherein,

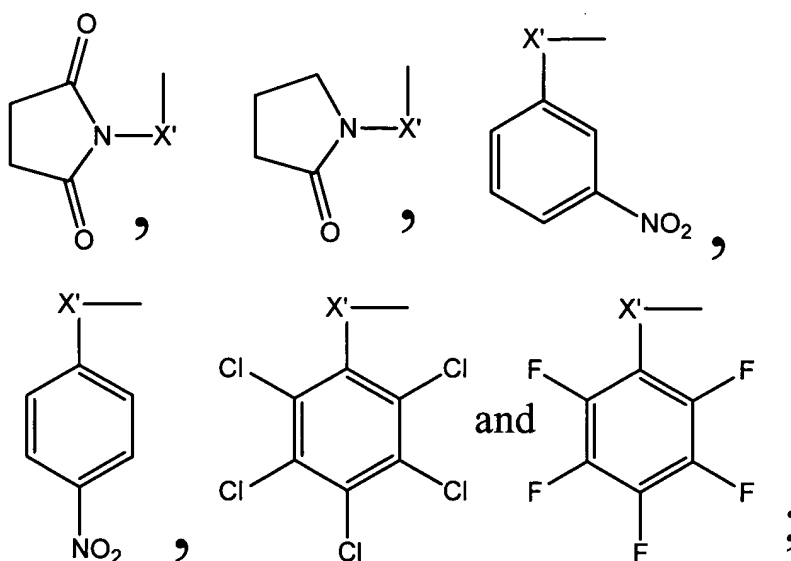
each carbon of the heterocyclic ring has the formula  $CJ_2$ ;

W is an atom or group that is located ortho, meta or para to the ring nitrogen and is NH,  $N-R^1$ ,  $N-R^2$ ,  $P-R^1$ ,  $P-R^2$ , O or S;

each J is the same or different and is H, deuterium (D),  $R^1$ ,  $OR^1$ ,  $SR^1$ ,  $NHR^1$ ,  $N(R^1)_2$ , fluorine, chlorine, bromine or iodine;

Z is O, S, NH or  $NR^1$ ; and

LG is an alcohol or thiol leaving group selected from the group consisting of:



wherein,

$X'$  is O or S;

$R^1$  is the same or different and is an alkyl group comprising one to eight carbon atoms which may optionally contain a heteroatom or a substituted or unsubstituted aryl group wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms; and

$R^2$  is an amino alkyl, hydroxy alkyl, thio alkyl group or a cleavable linker that cleavably links the reagent to a solid support wherein the amino alkyl, hydroxy alkyl or thio alkyl group comprises one to eight carbon atoms, which may optionally contain a heteroatom or a substituted or unsubstituted aryl group, and wherein the carbon atoms of the alkyl and aryl groups independently comprise linked hydrogen, deuterium and/or fluorine atoms; and

wherein the compound is isotopically enriched with one or more heavy atom isotopes.

72. (New) A method comprising:

- reacting an analyte with the compound of claim 71 to thereby produce a labeled analyte; and
- mixing the labeled analyte with one or more differentially labeled analytes.